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Docket No. T2315-907789

IN THE UNITED STATES PATENT & TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS & INTERFERENCES

Appellant: Raymond J. BERGERON, JR. :

Serial No.: 10/091,591 : Art Unit: 1614

Filed: March 27, 2002 : Examiner: Rebecca Cook

For: Method and Composition for the Treatment : Of Diarrhea and Gastrointestinal Spasms

RE-SUBMISSION OF BRIEF ON APPEAL

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The following Re-Submission of Brief on Appeal (as required under 37 CFR 1.192(c)) is submitted in support of the appeal of the Office Action mailed September 22, 2004, wherein the Examiner finally rejected claims 1-8, and in response to the Notification of Non-Compliant Appeal Brief mailed January 8, 2007..

It is noted that the Patent Appeals Specialist checked Box 1 on PTOL-462 (Rev. 7-05). A revised Brief containing the required headings (ix) Evidence Appendix and (x) Related Proceedings Appendix with the notation "None" under each is submitted herewith in triplicate.

The appeal brief fee of $250.00 was previously paid on February 22, 2005.

Please charge any fees associated with the filing of this paper to Deposit Account No. 50-1165 (Docket No. T2315-907789).

Respectfully submitted,

MILES & STOCKBRIDGE P.C.

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Filed: January 23, 2007

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REAL PARTY IN INTEREST

The real party in interest herein is the University of Florida Research Foundation, to which the above-captioned application is assigned.

RELATED APPEALS AND INTERFERENCES

The invention described in the claims on appeal herein is not related to the inventions described in the claims of any other application presently on appeal.

STATUS OF CLAIMS

The above-captioned application was filed with original claims 1-14. Claims 7-14 have been cancelled. This is an appeal from the final rejection of claims 1-6, all of the claims remaining in the application.

STATUS OF AMENDMENTS

An amendment after Final Rejection was filed 14 October 2004 and was entered by the examiner.

SUMMARY OF THE CLAIMED SUBJECT MATTER

Claim 1, the only independent claim on appeal, relates to anti-diarrheal, anti-secretory, or gastrointestinal anti-spasmodic pharmaceutical compositions comprising an anti-diarrheal or gastrointestinal antispasmodic (hereinafter "GI anti-spasmodic") effective amount of a polyamine (page 8, second full paragraph and page 11, second full paragraph – paragraph bridging pages 11 and 12) of the formula set forth below and a pharmaceutically acceptable carrier therefore:

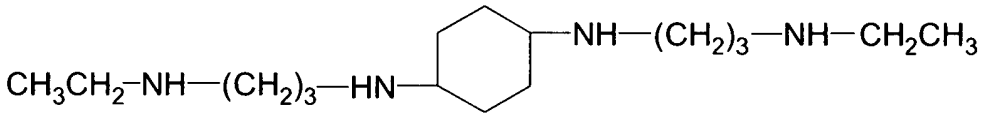
$$R_1\text{-}N^1(R_2)\text{-}(CH_2)x\text{-}N^2H\text{-}Q\text{-}N^3H\text{-}(CH_2)y\text{-}N^4(R_3)\text{-}R_4\text{----------(I)}$$

wherein: R_1, R_2, R_3 and R_4 may be the same or different and are H, alkyl, cycloalkyl or aralkyl having from 1 to 12 carbon atoms, or a heterocyclic group having from 3 to 10 atoms wherein the hetero atom is said N^1 or N^4 ;

Q is a cycloalkyl group having from 3 to 10 carbon atoms;

x is an integer from 3 to 6, inclusive;

excluding the trans isomers of the compounds having the structures:



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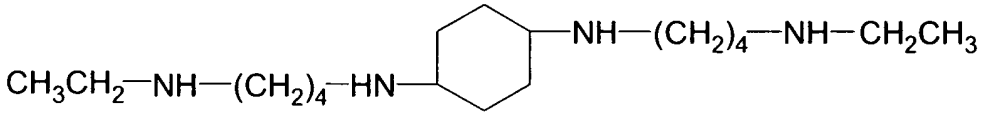


and y is an integer from 3 to 6, inclusive;

or (II) a salt thereof with a pharmaceutically acceptable acid (page 9, first full paragraph).

The present invention is predicated on the discovery that polyamines of the above formula act to inhibit the potential for the large and small intestines to contract. While not wishing to be bound by any theory as to the mechanism of action of the polyamines as inhibitors of this action of the intestines, it is hypothesized that the polyamines function via a receptor-dependent regulation mechanism whereby the myoelectric activity of the muscle tissue of the colon and small intestine and the secretion of fluid and electrolytes by these organs are

modulated. In addition, some of these above effects may be directly or indirectly mediated through the release of nitric oxide or through the activation of nitric oxide synthase.

ISSUES ON APPEAL

Claims 1-6 stand finally rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement.

An issue presented for appeal is whether the claim language employed, in particular, the "negative provisos", that render the claims non-inclusive of two species of polyamine that would otherwise be embraced by the claim's generic language, violate the requirements of 35 USC §112, first paragraph.

Claim 2 stands finally rejected under 35 USC §112, second paragraph, as failing to particularly point out and distinctly claim the invention on the ground that the "proviso" in claim 1 makes the phrase, "*trans* --- isomer", in claim 2 confusing.

An issue presented for appeal is whether the phraseology in claims 1 and 2 render them inconsistent.

Claims 1-8 stand finally rejected under 35 USC 103 as unpatentable over Bergeron [5,962,522].

A second issue presented for appeal is whether the Examiner has presented a prima facie case of obviousness of the claimed invention over Bergeron.

GROUPING OF CLAIMS

Appellant will concede that appealed claims 1-8 stand or fall together.

ARGUMENTS

The Rejection under 35 USC 112, First Paragraph

The Examiner is of the opinion that "the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention". Thus, the Examiner states at page 2 of the final Office Action:

> *"---No support is seen in the specification for the proviso 'excluding the trans isomers of the compounds having the structures' - There is nothing in the specification that would lead one to think that the recited compounds can be excluded, such as, cis is better than trans---".*

The current view of the courts is that there is nothing inherently ambiguous or uncertain about a negative limitation or an exclusionary proviso. So long as the boundaries of the patent protection sought are set forth definitely, albeit negatively, the claim complies with the requirements of 35 U.S.C. 112, second paragraph.

Moreover, an applicant is entitled to claim less than the invention contemplated by the original description thereof in the specification for whatever reason chosen by that applicant. Certainly, an applicant is not obliged to establish that the part of the invention disclaimed by the negative proviso claim language is somehow inferior to the invention left standing in the claim as suggested by the Examiner.

Thus, a claim which recited the limitation "not in excess of 10% . . . structure" in order to exclude the characteristics of the prior art product, was considered definite because each recited limitation was definite. In re Wakefield, 422 F.2d 897, 164 USPQ 636 (CCPA 1970).

In addition, a court found that the negative limitation, "incapable of forming a dye with said oxidized developing agent" was definite because the boundaries of the patent protection sought were clear. In re Barr, 444 F.2d 588, 170 USPQ 330 (CCPA 1971).

The MPEP [Section 2173.05(i)] states:

> *"---Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli, 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. Note that a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a prima facie case for lack of descriptive support. Ex parte Parks, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993). See MPEP 2163 - # 2163.07(b) for a discussion of the written description requirement of 35 U.S.C. 112, first paragraph---".*

It is respectfully submitted that the present claim language complies with the first paragraph of 35 U.S.C. 112 as interpreted by the MPEP and the Parks and Grasselli decisions. Moreover, attention is directed to the decision in In re Johnson, 223 USPQ 1260 holding that a claim to a genus with a recital of a negative proviso that did not appear in the specification complied with the description requirement. The negative proviso had the effect of excluding from the scope of the claim two species originally disclosed in the specification as within the invention, and was inserted to avoid having the claims read on a lost interference count. The claim recited a formula O-E-O-E', wherein E and E' were both positively defined, and ended "with the provisos that E and E' may not both include a divalent sulfone group and may not both include a divalent carbonyl group linking two aromatic nuclei." The proviso literally excluded more than the two species. The court stated:

> *"---The notion that one who fully discloses and teaches those skilled in the art how to make and use a genus and numerous species therewithin, has somehow*

> *failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of §112, first paragraph, appears to result in hypertechnical application of legalistic prose relating to that provision of the statute---".*

The court had another opportunity to review "the sort of 'hypertechnical application' of the written description requirement of §112 criticized in [Johnson]" in In re Driscoll, 195 USPQ 434, 438. In holding that a disclosure of a group of chemical compounds containing a plurality of groups defined by Markush terminology, one of which groups contained 14 members, described the same group of compounds otherwise identical except that the 14-member group was now limited to only one of the members, the court stated:

> *"---Were the board's decision permitted to stand, future applicants, particularly in cases of this nature, would in all likelihood find themselves in the predicament reflected in the following observation by Judge Learned Hand: 'If, when [applicants] yield any part of what they originally believed to be their due, they substitute a new "invention," only two courses will be open to them: they must at the outset either prophetically divine what the art contains, or they must lay down a barrage of claims, starting with the widest and proceeding by the successive incorporation of more and more detail, until all combinations have been exhausted which can by any possibility succeed. The first is an impossible task; the second is a custom already more honored in the breach than in the observance, and its extension would only increase that surfeit of verbiage which has for long been the curse of patent practice, and has done much to discredit it. It is impossible to imagine any public purpose which it would serve'---".*

It is impossible to quarrel with the above holdings in the Johnson and Driscoll decisions. Indeed, it is doubtful that an inventor, ignorant of the precepts and nuances of patent law, after discovering that a species or a subgenus of a genus that he regards as his invention is old or obvious, would not believe that he *possessed*, at the time he invented the genus, that genus minus the old or obvious species or subgenus. In Johnson, the inventors were permitted to exclude the old or obvious species, ostensibly because they literally disclosed these species in their specification. The fact that Johnson actually excluded somewhat more than the two

species was seemingly unimportant to the court, since this fact was relegated to a footnote that had no discussed bearing on the court's decision.

Applicants certainly have the right to claim less than the whole of their invention, provided that the part of the invention claimed is definitively and clearly claimed.

In *In re Voss*, 194 USPQ267 the federal court, in order to decide whether the Examiner could rely on a French patent as a reference, had to first decide whether applicant complied with 35 USC 112, first paragraph, with respect to those claims. The court stated:

> *"---How the application of the parent achieves compliance is immaterial. In re Smith, 481 F.2d 910, 178 USPQ620 (CCPA 1973). It is only required, for example, that the specification describe the invention sufficiently for those of ordinary skill in the art to recognize that the applicant invented the subject matter he 'now claims'. In re Smythe, 480 F.2d 1376, 1382, 178 USPQ 279, 284 (CCPA 1973). The PTO has the initial burden of presenting evidence or reasons why those skilled in the art would not recognize in the specification a description of the invention defined by the present claims. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976). ---*
>
> *the expression "at least 50%" crystal content does not literally appear in appellant's parent application. However, the mere lack of literal support is not enough to carry the PTO's initial burden. In re Wertheim, supra at 265, 191 USPQ at 98. Nor is this a situation where the claims read on embodiments outside the scope of the description. Appellant's parent application describes the invention in terms broader than those in the claim,---"*

See also Ex parte Drewe, 203 USPQ1127 and In re Eickmeyer, 202 USPQ 655. In Eickmeyer, the court stated:

> *"---the dispositive issue is whether there is support (satisfying the description requirement of section 112, first paragraph) in appellant's specification and in the parent applications for the claimed temperature limitation of 'at least about 56° C.'. As (the court) read the board's opinion, (a) base for its rejections: (1) that appellant has not disclosed any minimum temperature far the operation of the process, that is, he has not shown that 56°C is a minimum or critical lower limit far the operation of the process.--- Regarding the first basis, the PTO has cited ---no precedent for requiring appellant to demonstrate that his process will not operate below 56°C, to satisfy the description requirement of section 112, first paragraph; an application must contain sufficient disclosure, expressly or*

inherently, to make it clear to one skilled in the art that the appellant was in possession of the subject matter claimed, In re Matt, 539 F.2d 1291, 190 USPQ 536 (CCP A 1976); In re Smythe, 480 F,2d 1376" 178 USPQ 279' (CCPA 1973), "[A) statement of appellant's invention [in his specification] which is as broad as appellant's broadest claims" is sufficient to meet this requirement- In re Robbins, 57 CCPA 1321, 1325-26, 429 F,2d 452, 456, 166 USPQ 552, 555 (CCPA 1970). Appellant's specification indicates that hat potassium carbonate solutions are mown in the prior art and contains replicate tests of the operation of his process at 56°C. Thus, that appellant considered his hat system to operate "at an elevated temperature of at least about 56°C." would have been clear to. one skilled in the art from the replicate tests at 56° and 80°C and the teachings of the prior art that such systems were known to operate at temperatures above 80^0 C, although appellant may be entitled to claim a range of temperatures below 56°C, he need not claim all that he is entitled to claim and need have support only far what he does claim. We are not persuaded that there is any requirement far appellant to demonstrate the criticality of a lower limit to meet the description requirement. And a review of the parent applications indicates that language corresponding to that in appellant's specification was also present in all of the parent applications relied upon for applicant s chain of priority---In view of the foregoing, we hold that the limitation "at an elevated temperature of at least. about 56° C." is fully described in appellant's specification and in the parent applications---" (emphasis added).

Thus, it is apparent that the great weight of authority is in favor of permitting an applicant to claim less than he/she is entitled to by the use of negative provisos where, to do so does not do violence to the disclosure in the specification. In the present case, applicant should clearly be permitted to disclaim by negative proviso several species encompassed by the original claim language, if for no other reason but that the prior art discloses those species.

Accordingly, a reversal of this ground of rejection is respectfully requested.

The Rejection under 35 USC 112, Second Paragraph

Considerable confusion concerning this ground of rejection has arisen since issuance of the Final Office Action. Appellant filed an amendment after the final rejection seeking to resolve some of the issues raised therein. On November 26, 2004 the Examiner issued an Advisory Action stating:

"*---Applicant's arguments regarding the rejections under 35 use 112, paragraph*

> *one and 35 use 103(a) have been considered but are not persuasive for the reasons given in the Paper of September 22, 2003. The MPEP 2173.05(i) states that any limitation which does not have a basis in the original disclosure should be rejected under 35 use 112, first paragraph as failing to comply with the written description requirement. No support is seen in the specification for the two structures that are now excluded by proviso. Applicant has not presented a showing of unexpected results for the cis-isomer of the trans-compound disclosed by Bergeron---".*

Since the Advisory Action mentions only the 35 USC 112, first paragraph, and 35 USC 103(a) grounds of rejection as not being overcome by the amendment after final rejection, appellant assumed that the 35 USC 112, second paragraph rejection had been overcome thereby. A second advisory action ["Notification of Non-Compliant Appeal Brief"] was issued by the Examiner on May 27, 2005 indicating that appellant's assumption regarding the 35 USC 112, second paragraph rejection having been withdrawn was erroneous. Accordingly, appellants argue as follows regarding the invalidity of this ground of rejection

The Examiner alleges that claims 1 and 2 are now inconsistent because of the negative provisos in claim 1 and the reference to *trans* isomers in claim 2. Claim 1, however, does not exclude all *trans* isomers; only the two specified in the proviso. Since claim 2 is dependent on claim 1, it inherently also excludes these two isomers. The fact that claim 2 refers to other *trans* isomers does not, therefore, render it inconsistent in any way with claim 1.

Accordingly a reversal of this ground of rejection is respectfully requested.

The Rejection under 35 USC 103

The Examiner stated in the Final Office Action:

> *"---Bergeron (Table 1, compounds 33 and 34) discloses the compounds differing from the compounds of the compositions of claims 1-6 by a proviso that excludes the trans compound of Bergeron. The instant dependent claims 4-6 differ over Bergeron in reciting a compound in which x and y is 3 are 3 as compared to Bergeron where x and y are 4. The instant claims further differ over Bergeron in disclosing a composition suitable for treating diarrhea. However, in the absence*

of a showing of unexpected results, no unobviousness is seen in one isomer over the other. In re Adamson et al. 125 USPQ 233.

Furthermore, because the characteristics normally possessed by members of a homologous series are principally the same, varying gradually from member to member, one of ordinary skill in the art would know what to expect in adjacent members so that a mere difference in degree is not the marked superiority which will ordinarily remove the unpatentability of adjacent homologues of old substances. In re Henze 85 USPQ 261.

Moreover, Bergeron (column 20, lines 40-45) discloses that the polyamine derivatives of Table 1 were diluted in sterile water, a pharmaceutically acceptable carrier. Thus, Bergeron discloses a composition comprising a compound of claim 8 in a pharmaceutically acceptable carrier. Applicant argues that the composition of Bergeron is not a "pharmaceutical composition." This is not persuasive. There is no evidence on the record to prove that the composition of Bergeron does not necessarily or inherently possess the characteristics of the instant composition.

The Examiner thus admits that the compounds present in the claimed composition are novel over those disclosed by Bergeron, but argues that Bergeron nevertheless discloses pharmaceutical compositions containing compounds so analogous to those of the claims as to raise a presumptive *prima facie* case of obviousness thereover.

The Examiner's logic is fatally flawed, however, in that Bergeron does not disclose any pharmaceutical compositions containing the so-called analogous compounds 33 and 34 of Table 1. Compounds 33 and 34 are indeed the *trans*-isomers of two of the polyamines embraced by the compositions of the present invention and applicant will admit that, on the face of it, the *trans* isomers are analogous to the *cis*-isomers of the same polyamines. However, the Examiner is greatly mistaken in stating that Bergeron discloses pharmaceutical compositions for treating diarrhea or gastrointestinal spasms or any other pathological condition for that matter.

The Examiner is correct in stating that Bergeron discloses solutions of compounds 33 and 34 in sterile water; however, these solutions are not

"pharmaceutical compositions" as specified in the rejected claims. The Bergeron "compositions" are merely solutions of the compounds suitable for screening the compounds for "their 48 and 96 hour IC_{50} values in L1210 cell culture assays" (col. 19, lines 35-38, emphasis added). Applicant is aware of no authority, nor has the Examiner cited any, for the proposition that a solution suitable for an in vitro assay is equivalent to or even suggestive of a pharmaceutical composition. The present claims are drawn to "pharmaceutical compositions suitable for administration to a human or nonhuman animal in need thereof". Nowhere in the reference is there a disclosure or suggestion of such a composition containing either compound 33 or 34. Certainly, the mere disclosure of a "screening solution" useful for an in vitro cell culture assay is not tantamount to such a disclosure.

Secondly, the reference discloses no specific amounts of either compound 33 or 34 present in the screening solutions. Thus, the skilled artisan is provided with no insight as to any amount of compound to place in solution, much less an amount effective to achieve an anti-diarrheal effect in a therapeutic setting. It is of course well settled in the law that a reference must enable the practice of a claimed invention before it can be said to disclose or suggest the invention. In re Legrice, 133 USPQ 365; Phillips v. Ladd, 138 USPQ 421; Dupont v. Ladd, 140 USPQ 297; In re Brown, 141 USPQ 245; In re Foster, 145 USPQ 166; In re Dow, 5 USPQ2d 1529.

It is apparent that one skilled in the art would be unable to prepare any composition containing either compound 33 or 34, based on the information contained in Bergeron since no amounts of the compounds are set forth.

Since the present claims specify amounts of the compounds effective to treat diarrhea, for example, and the reference relied upon sets forth no amounts whatsoever, it cannot be said to anticipate the invention. It is, of course, well settled that "a prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without undue

experimentation" (Minnesota Mining and Manufacturing Co. v. Chemique, Inc. 303 F3d 1294, 64 USPQ2d 1270 (Fed. Cir. 2002)).

In *In re Wands*, 858 F2d 721, 8 USPQ2d 1400 (Fed. Cir. 1998), it is stated that the factual premises of enablement in a prior art reference may include the following:

(1.) the quality of experimentation necessary;

(2.) the amount of direction and guidance given;

(3.) the nature of the invention;

(4.) the state of the prior art;

(5.) the relative skill of those in the art;

(6.) the predictability or unpredictability of the art; and

(7.) the breadth of the claims.

It is readily apparent that the reference relied upon fails on all seven counts to qualify as an enabling disclosure of the claimed invention since no amounts of the critical compounds are set forth. See also In re Grose, 201 USPQ 57, and In re Wiggins, 179 USPQ 421.

Attention is also directed to the decision in Elan Pharmaceuticals Inc. v. Mayo Foundation for Medical Education and Research, 68 USPQ2d 1373 (CAFC, Nov., 2003) wherein the CAFC held that the disclosure of an assertedly anticipating prior art reference must be adequate to enable possession of desired subject matter, and a reference that merely names or describes the desired subject matter thus does not anticipate it if the subject matter cannot be produced without undue experimentation, stating:

> *"---To serve as an anticipating reference, the reference must enable that which it is asserted to anticipate. 'A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.' [Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1354,*

65 USPQ2d 1385, 1416 (Fed. Cir. 2003). See Bristol-Myers Squibb v. Ben Venue Laboratories, Inc., 246 F.3d 1368, 1374, 58 USPQ2d 1508, 1512 (Fed. Cir, 2001) ('To anticipate the reference must also enable one of skill in the art to make and use the claimed invention.'); PPG Industries, Inc. v. Guardian Industries Corp., 75 F.3d 1558, 1566, 37 USPQ2d 1618, 1624 (Fed. Cir. 1996) ('To anticipate a claim, a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.') ---Enablement requires that 'the prior art reference must teach one of ordinary skill in the art to make or carry out the claimed invention without undue experimentation.' [Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1369, 52 USPQ2d 1129, 1134 (Fed. Cir. 1999) ('Whether undue experimentation would have been required to make and use an invention, and thus whether a disclosure is enabling under 35 U.S.C. § 112, 11, is a question of law that we review de novo, based on underlying factual inquiries that we review for clear error.')]. (See also) In re Goodman, 29 USPQ2d 2010, 2015 (Fed. Cir, 1993). --- The principles underlying application of the criteria of enablement to the content of the prior art were discussed in In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985): 'It is well settled that prior art under 35 U.S.C. § 102(b) must sufficiently describe the claimed invention to have placed the public in possession of it. Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed invention. Accordingly, even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it is not enabling. It is not, however, necessary that an invention disclosed in a publication shall have actually been made in order to satisfy the enablement requirement.' Id. at 533, 226 USPQ at 621. See also In re Borst, 345 F.2d 851, 855, 145 USPQ 554, 557 (CCPA 1962) ('the disclosure must be such as will give possession of the invention to the person of ordinary skill. Even the act of publication or the fiction of constructive reduction to practice will not suffice if the disclosure does not meet this standard.'). ---The determination of what level of experimentation is "undue," so as to render a disclosure non-enabling, is made from the viewpoint of persons experienced in the field of the invention. See Enzo Biochem, supra: 'The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art.' In re Wands, 8 USPQ2d 14001 (Fed. Cir. 1988). In Wands the court observed that '[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed' quoting In re Jackson, 217 USPQ 804, 817---"

Clearly, the weight of authority supports the proposition that a reference that does not enable one skilled in the art to possess what is allegedly disclosed does not disclose it within the meaning of the patent laws. Since Bergeron does not enable a solution or composition containing either compound 33 or 34, the reference cannot be said to anticipate, either expressly or inherently, any pharmaceutical composition containing either of the compounds. Stated differently, a nonenabled disclosure cannot be said to anticipate anything.

Attention is also directed to the decision in In re Gangadharam 13 USPQ2d 1568 (CAFC, 1989), wherein the court held that the disclosure of in vitro test was insufficient on which to reject claims drawn to an in vivo utility. What makes that decision extremely relevant to the present fact situation is that in Gangadharam, at least the in vitro and in vivo tests were related; still, the court held that the former did not suggest or anticipate the latter. In the present case, the respective tests are not even remotely related; one being concerned with IC_{50} values in a L1210 cell culture assay and the other to an antidiarrheal pharmaceutical composition. Certainly, if the in vitro test in Gangadharam was insufficient to anticipate the related in vivo utility, the in vitro test of the reference is insufficient to anticipate the completely unrelated related in vivo utility of the present claims.

Accordingly, a reversal of this ground of rejection is respectfully requested.

It is also clear from the Board's previous decision in this case (Paper no. 19) that the above-stated new ground of rejection was not intended to apply to claims that did not include compounds 33 or 34 of the Bergeron reference. Thus, the Board went to great lengths to emphasize that then dependent claims 2-7 were included in the rejection solely because applicant had stated in his Brief that all of the claims would stand or fall together. Since the rejection is based on 35 USC § 102(b) and the Examiner and Board agreed that compounds 33

and 34 of the reference were the only compounds disclosed that were encompassed by the claims, present claims 1-6, which specifically exclude these two compounds are not subject to rejection over Bergeron under §103.

To the extent that the Examiner relies on the decision in *In re Henze*, 85 USPQ 261 it is respectfully pointed out that *Henze* was overruled by the decision in *In re Stemniski*, 170 USPQ 343.

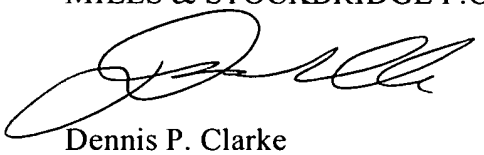
Accordingly, a reversal of this ground of rejection is respectfully requested.

CONCLUSION

It is respectfully requested that the final rejection of record be reversed and the application remanded to the Examiner for immediate allowance.

Respectfully submitted,

MILES & STOCKBRIDGE P.C.



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Date: January 23, 2007

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EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

None.

APPENDIX OF CLAIMS ON APPEAL – SERIAL NO. 10/091,591

1. An anti-diarrheal or gastrointestinal anti-spasmodic pharmaceutical composition comprising [A] an effective amount of a compound having the formula:

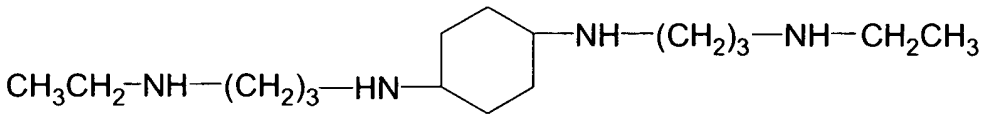
$$R_1\text{-}N^1(R_2)\text{-}(CH_2)x\text{-}N^2H\text{-}Q\text{-}N^3H\text{-}(CH_2)y\text{-}N^4(R_3)\text{-}R_4 \qquad (I)$$

wherein: R_1, R_2, R_3 and R_4 are the same or different and are H, alkyl, cycloalkyl or aralkyl having from 1 to 12 carbon atoms, or a heterocyclic group having from 3 to 10 atoms wherein the hetero atom is said N^1 or N^4;

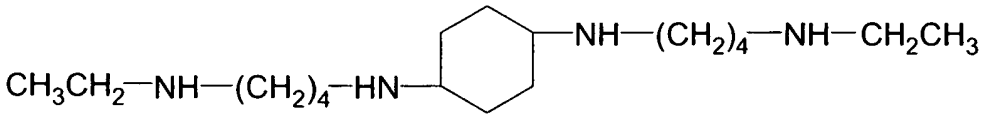
Q is a cycloalkyl group having from 3 to 10 carbon atoms;

x is an integer from 3 to 6, inclusive;

excluding the *trans* isomers of the compounds having the structures:



and



and y is an integer from 3 to 6, inclusive;

or (II) a salt thereof with a pharmaceutically acceptable acid; and [B] a pharmaceutically acceptable carrier therefor.

2. The composition according to claim 1 wherein Q is connected either *cis* or *trans* as the (1,2), (1,3), (1,4), (1,5) or (1,6) isomer.

3. The composition according to claim 1 wherein Q is cyclohexyl.

4. The composition according to claim 1 wherein x is 3 and y is 3.

5. The composition according to claim 1 wherein x is 3, y is 3, R_1 and R_3 are both H and R_2 and R_4 are both ethyl.

6. The composition according to claim 1 wherein Q is cyclohexyl; x and y are 3; R_1 and R_3 are both H, and R_2 and R_4 are both ethyl.